



Estimating the burden of disease attributable to high blood pressure in South Africa in 2000

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Objectives. To estimate the burden of disease attributable to high blood pressure (BP) in adults aged 30 years and older in South Africa in 2000.

Design. World Health Organization comparative risk assessment (CRA) methodology was followed. Mean systolic BP (SBP) estimates by age and sex were obtained from the 1998 South African Demographic and Health Survey adult data. Population-attributable fractions were calculated and applied to revised burden of disease estimates for the relevant disease categories for South Africa in 2000. Monte Carlo simulation-modelling techniques were used for uncertainty analysis.

Setting. South Africa.

Subjects. Adults aged 30 years and older.

Outcome measures. Mortality and disability-adjusted life years (DALYs) from ischaemic heart disease (IHD), stroke, hypertensive disease and other cardiovascular disease (CVD).

Results. High BP was estimated to have caused 46 888 deaths (95% uncertainty interval 44 878 - 48 566) or 9% (95% uncertainty interval 8.6 - 9.3%) of all deaths in South Africa in 2000, and 390 860 DALYs (95% uncertainty interval 377 955 - 402 256) or 2.4% of all DALYs (95% uncertainty interval 2.3 - 2.5%) in South Africa in 2000. Overall, 50% of stroke, 42% of IHD, 72% of hypertensive disease and 22% of other CVD burden in adult males and females (30+ years) were attributable to high BP (systolic BP \geq 115 mmHg).

Conclusions. High BP contributes to a considerable burden of CVD in South Africa and results indicate that there is considerable potential for health gain from implementing BP-lowering interventions that are known to be highly cost-effective.

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High blood pressure (BP) is responsible for a large and increasing proportion of the burden of disease. Its impact is now recognised as global, and it is one of the leading causes of disease in middle-income countries and of emerging importance in low-income countries. Globally, analyses indicate that about two-thirds of strokes and almost half of all ischaemic heart disease (IHD) cases are attributable to raised BP (systolic BP \geq (SBP) 115 mmHg).¹

It has also become increasingly evident that the association between BP and stroke, IHD and renal failure is direct and continuous from relatively low levels.²⁻⁴ In fact, the majority

of disease associated with BP and other continuous risk factors, such as cholesterol level and body weight, occurs in people with suboptimal levels below the thresholds set for hypertension, hypercholesterolaemia or obesity.

The 1998 South African Demographic and Health Survey (SADHS)⁵ provided nationally representative data on hypertension. The mean SBP for those over the age of 15 years was 123 mmHg for men and 119 mmHg for women.⁶ The prevalence of hypertension (BP greater than 140 mmHg systolic and/or 90 mmHg diastolic using the current World Health Organization (WHO) cut-off) was 21%, and 25% when age-standardised to the world population.⁶ The degree of urbanisation among black Africans predisposes to the development of hypertension,⁷ suggesting that it may increase with continued trends towards urbanisation. Using the former WHO cut-off of 160/95 mmHg, the SADHS also showed that 26% of hypertensive men and 38% of hypertensive women had their BP controlled indicating considerable underdiagnosis and treatment.⁵ Further analysis revealed that the poorer, younger men, without health insurance had the worst level of hypertension control.⁸

This article uses existing SADHS data on prevalence in adults aged 30 years and older to quantify adverse health consequences associated with high BP, and to estimate the burden of disease attributed to high BP by sex and age group in South Africa for the year 2000.

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Methods

Using WHO comparative risk assessment (CRA) methodology,^{9,10} the disease burden attributable to a particular risk factor is estimated by comparing the current local health status with a theoretical minimum counterfactual with the lowest possible risk. The population-attributable fraction (PAF) of disease burden in a population is determined by the prevalence of exposure to the risk factor in the population, and the relative risk (RR) of disease occurrence given exposure.

SBP in mmHg usually rises steadily with age. In contrast, diastolic BP (DBP) increases through the 4th or 5th decade, but then plateaus and begins to decline in the 6th and 7th decades, making SBP or pulse pressure (the difference between the two) better predictors for future adverse events than DBP. SBP was therefore chosen because data are widely available for this index of BP, and it appears to be a good predictor of cardiovascular disease (CVD).¹

The outcomes selected were those assessed in the WHO global CRA study by Lawes *et al.*¹ based on consistent direct and continuous associations in cohort studies and evidence from randomised clinical trials, and included stroke, IHD, hypertensive disease and other CVD. Other CVD does not include heart failure, pulmonary oedema and cardiac arrhythmias since these conditions have been redistributed across specified cardiovascular outcomes in the South African National Burden of Disease Study.¹¹ Data suggested causal relationships with renal failure, but since this could not be mapped to a burden of disease outcome, it was not included in the global study,¹ or in this one.

Estimates of mean SBP and standard deviations (SD) by age and sex for adults aged 30 years and older were obtained from a re-analysis of the 1998 SADHS data.⁵ BP was measured electronically in the 1998 SADHS, in part because initial training in the pilot study highlighted the need for a more automated process for fieldworkers with limited clinical skills to achieve accurate BP readings. BP measurements were taken after the participant had been seated for 5 minutes using an Omron M1 electronic BP manometer (Omron Life Science Co. Ltd, Tokyo Japan). BP and pulse were taken 3 times on the left arm with the palm upward.⁶ If the second measurement differed by more than 5 mmHg from the first, the first reading was excluded.⁶ Confidence intervals (CIs) around mean SBP estimates were calculated to reflect the sampling error. Use of the Omron electronic manometer rather than the auscultatory method using a mercury sphygmomanometer was motivated by the recommendation of international bodies and extensive validation testing of these instruments.^{6,12-14}

In the WHO global CRA study,¹ data on risk factor-disease relationships were obtained from the Asia-Pacific Cohort Studies Collaboration (APCSC) data for 2001. In the present analysis, however, we used risk ratios obtained from a

collaborative meta-analysis of individual participant data from 61 separate prospective studies. In the Prospective Studies Collaboration,¹⁵ information was obtained on each of 1 million adults with no previous vascular disease, recorded at baseline in prospective observational studies of blood pressure and mortality. Hazard ratios in each decade of age associated with a 20 mmHg lower usual SBP at the start of that decade are presented in Table 1 for stroke, IHD, hypertensive disease and other CVD mortality together with ICD-9 codes.¹⁶ At ages 40 - 69 years, each difference of 20 mmHg usual SBP was associated with more than a twofold difference in the death rate from stroke, and with twofold differences in death rates from IHD and other CVD.¹⁵

There was attenuation of proportional associations with age for all outcomes, and these were about half as extreme at ages 80 - 89 as at ages 40 - 49.¹⁵ Age-specific associations were similar for men and women, and hence it was not necessary to have sex-specific estimates for CRA. Age-specific associations were also similar for cerebral haemorrhage and cerebral ischaemia, and hence all types of stroke were considered in this analysis.

Regression dilution bias has particular relevance in observational studies of BP. This bias occurs since baseline or 'one-off' measures of BP are subject to random fluctuations, due partly to the measurement process, and partly to real but temporary deviations from the 'usual' exposure level. Consequently, baseline exposure values have a wider distribution than the 'usual' exposure values, and with repeated measures there is a 'regression to the mean' of values whereby an initially extreme observation tends to become less abnormal with replication. This bias is accounted for in the estimates of RR,^{15,17} and needs also to be reflected in a narrower distribution around mean SBP levels. Hence this analysis involved correction for 'time-dependent' regression dilution,¹⁵ and observed SDs around mean SBP levels in SADHS 1998 data were corrected using the published correction dilution ratios.¹⁵

Customised MS Excel spreadsheets based on templates used in the Clinical Trials Research Unit (CTRU) at the University of Auckland (S Vander Hoorn, University of Auckland - personal communication, 2005) as well as Australian studies (T Vos, University of Queensland - personal communication, 2005) were used to calculate the attributable burden using a discrete version of the general potential impact fraction (see below), taking into account continuous risk factor-disease exposures compared with a theoretical minimum distribution (conferring the lowest possible risk) on a categorical scale.

$$PAF = \frac{\sum_{i=1}^n P_i RR_i - \sum_{i=1}^n P'_i RR_i}{\sum_{i=1}^n P_i RR_i}$$



where n = the number of exposure categories; P_i = the proportion of population in exposure category i ; RR_i = the relative risk for exposure category i ; and P'_i = the proportion of population in exposure category i in the counterfactual distribution.

The theoretical minimum exposure distribution is zero in most cases, since zero exposure reflects minimum risk (e.g. no smoking). For high BP, however, zero exposure would be physiologically impossible, and therefore is an inappropriate choice as the theoretical minimum. The theoretical minimum of SBP was estimated to be a mean of 115 mmHg and SD of 6 mmHg for all age and sex groups. This theoretical minimum is based on the SBP level down to which epidemiological relationships with cardiovascular outcomes are observed, and is also consistent with levels of SBP in populations with little or no CVD. Recent data from clinical trials have also indicated a reduction in stroke after lowering SBP by 10 mmHg in participants with a mean SBP of 125 mmHg.¹

The PAFs were then applied to revised South African burden of disease estimates for 2000,¹⁸ deaths, years of life lost (YLLs), years of life lived with disability (YLDs) and disability-adjusted life years (DALYs) for the relevant disease categories to calculate attributable burden.

Monte Carlo simulation-modelling techniques were used to present uncertainty ranges around point estimates that reflect all the main sources of uncertainty in the calculations. We used the @RISK software version 4.5 for Excel,¹⁹ which allows multiple recalculations of a spreadsheet, each time choosing a value from distributions defined for input variables. Normal probability distributions were specified around the mean SBP by age and sex. For the RR input

variables a normal distribution was specified, with the natural logarithm of the RR estimates as the entered means of the distribution and standard errors derived from the published 95% CIs (Table I). For each of the output variables (namely attributable burden as a percentage of total burden in South Africa in 2000), 95% uncertainty intervals were calculated bounded by the 2.5th and 97.5th percentiles of the 2000 iteration values generated.

Results

Table II shows the mean SBP by age and sex and corrected SDs using age-specific correction ratios. Mean SBP increased with age and was higher in men than in women across all ages, excepting the 70 - 79 and 80+ age groups in which mean SBP was higher in women than in men.

The PAFs for high BP are shown for males and females by age group in Table III for all the related outcomes. PAFs were higher in men under the age of 70, and higher in women in the 70+ age group. Overall, about 42% of IHD burden in adults aged 30 years and older was attributable to SBP \geq 115 mmHg. PAFs for stroke were higher than for IHD for both males and females. Fifty-one per cent of stroke in males and 48% in females was attributable to SBP \geq 115 mmHg. In both males and females stroke PAFs peaked in the 60 - 69-year age group at above 60%, with a downward trend thereafter. A similar pattern is noticed for IHD, but with lower attributable fractions. About 24% and 20% of other CVD and 73% and 71% of hypertensive disease was attributable to SBP \geq 115 mmHg in males and females, respectively.

High BP was estimated to cause 46 888 deaths (95% uncertainty interval 44 878 - 48 566), accounting for 9% (95% uncertainty interval 8.6 - 9.3%) of all deaths in South Africa in 2000

Table I. Age-specific hazard ratios* (95% CI) for each 20 mmHg decrease in usual SBP

| Related health outcome | ICD-9 codes | Age (yrs) | | | | |
|--|--------------------------|--------------------|--------------------|--------------------|--------------------|--------------------|
| | | 30 - 44 | 45 - 59 | 60 - 69 | 70 - 79 | 80+ |
| Ischaemic heart disease | 410 - 414 | 0.49 (0.45 - 0.53) | 0.50 (0.49 - 0.52) | 0.54 (0.53 - 0.55) | 0.60 (0.58 - 0.61) | 0.67 (0.64 - 0.70) |
| Stroke | 430 - 438 | 0.36 (0.32 - 0.40) | 0.38 (0.35 - 0.40) | 0.43 (0.41 - 0.45) | 0.50 (0.48 - 0.52) | 0.67 (0.63 - 0.71) |
| Hypertensive disease (includes essential hypertension, hypertensive heart and/or renal disease) [†] | 401 - 405 | 0.19 (0.17 - 0.22) | 0.20 (0.18 - 0.23) | 0.22 (0.20 - 0.25) | 0.25 (0.23 - 0.28) | 0.31 (0.29 - 0.33) |
| Other cardiovascular diseases (e.g. conduction disorders, constrictive pericarditis) | 417, 423, 426, 457 - 459 | 0.43 (0.38 - 0.48) | 0.50 (0.47 - 0.54) | 0.53 (0.51 - 0.56) | 0.64 (0.61 - 0.67) | 0.70 (0.65 - 0.75) |

*Hazard ratios from the Prospective Studies Collaboration¹⁵ and converted to correspond with the global burden of disease age categories (S Vander Hoorn - personal communication).
[†]For hypertensive disease, 95% CIs by age were estimated using the variation or the difference in the excess risk relative to the size of the excess risk for the hypertensive disease all-age estimates published by Prospective Studies Collaboration.¹⁵
 ICD-9 = International Classification of Diseases, 9th revision.¹⁶



Table II. Estimates of age-specific mean systolic blood pressure (SBP) and standard deviations (SDs) (mmHg) for males and females in South Africa, 2000, and regression/dilution ratios by age

| Parameter | Age (yrs) | | | | |
|----------------------------------|-------------|-------------|-------------|-------------|-------------|
| | 30 - 44 | 45 - 59 | 60 - 69 | 70 - 79 | 80+ |
| Males | | | | | |
| Mean SBP | 122 | 130 | 138 | 140 | 139 |
| SD* | 11 | 13 | 14 | 13 | 11 |
| Females | | | | | |
| Mean SBP | 116 | 128 | 137 | 141 | 144 |
| SD* | 13 | 13 | 14 | 14 | 13 |
| Regression/dilution ratio | 0.67 | 0.62 | 0.58 | 0.54 | 0.49 |

*Corrected by regression/dilution ratio from the Prospective Studies Collaboration.¹⁵

Table III. High blood pressure population-attributable fractions (%) for selected health outcomes by age and sex, South Africa, 2000

| Health outcome | Age (yrs) | | | | | |
|-------------------------------|-----------|---------|---------|---------|------|------|
| | 30 - 44 | 45 - 59 | 60 - 69 | 70 - 79 | 80+ | 30+ |
| Males | | | | | | |
| Ischaemic heart disease | 23.3 | 41.6 | 51.7 | 48.3 | 37.9 | 41.9 |
| Stroke | 32.5 | 53.8 | 63.8 | 59.5 | 37.9 | 51.3 |
| Hypertensive disease | 49.1 | 74.7 | 85.3 | 84.6 | 76.3 | 72.7 |
| Other cardiovascular diseases | 15.8 | 26.3 | 35.9 | 27.9 | 20.9 | 24.1 |
| Females | | | | | | |
| Ischaemic heart disease | 11.7 | 37.5 | 50.3 | 49.3 | 44.0 | 41.5 |
| Stroke | 17.0 | 49.2 | 62.3 | 60.7 | 44.0 | 48.4 |
| Hypertensive disease | 28.2 | 70.4 | 84.3 | 85.8 | 82.9 | 70.9 |
| Other cardiovascular diseases | 7.5 | 23.1 | 34.6 | 28.7 | 25.2 | 19.5 |
| Persons | | | | | | |
| Ischaemic heart disease | 19.8 | 40.1 | 51.1 | 48.8 | 42.0 | 41.7 |
| Stroke | 24.6 | 51.2 | 62.9 | 60.3 | 42.3 | 49.6 |
| Hypertensive disease | 36.8 | 72.2 | 84.6 | 85.5 | 81.4 | 71.5 |
| Other cardiovascular diseases | 11.2 | 24.7 | 35.2 | 28.4 | 23.6 | 21.6 |

(Table IV). In total, there were more attributable deaths and DALYs in females than in males, and BP accounted for 11.2% of all female and 7.0% of all male deaths in South Africa in 2000. In males, IHD accounted for the most deaths, but the DALYs for stroke were higher than those for IHD because of the greater disability component for stroke. In women, both stroke deaths and DALYs were highest. Since most BP-related deaths and non-fatal events occur in middle age and in the elderly, the loss of healthy life years comprised a smaller proportion of the total: 390 860 DALYs (95% uncertainty interval 377 955 - 402 256) or 2.4% of all DALYs (95% uncertainty interval 2.3 - 2.5%) in South Africa in 2000.

Although the same age-specific hazard ratios were used for males and females for each outcome, when comparing the burden (or DALYs) attributable to high BP it is clear that there is a marked difference between males and females (Fig. 1). In men, IHD and stroke account for similar proportions (about 38%) of the total attributable burden, but in women stroke accounts for the highest proportion (43.0%), followed by hypertensive disease (30.2%), with IHD accounting for only 23.6% of the burden attributable to high BP (Fig. 1).

There are more attributable deaths in males in the younger age groups, but in older persons (60+ years of age) there are more female than male-attributable deaths. For males, attributable deaths peaked at 70 - 79 years, with a decline in the 80+ age group. For females the peak is in the 80+ age group (Fig. 2).

Discussion

This study estimates that in the year 2000, almost 47 000 deaths in South Africa were attributed to high BP, accounting for about 9% of all deaths and contributing to 2.4% of total DALYs. Worldwide, high BP is estimated to cause 7.1 million deaths (12.8% of total) and 64.3 million DALYs (4.4% of the total burden).¹ In South Africa, high BP was the second leading risk factor in terms of deaths, following sexually transmitted diseases resulting from unsafe sex, which accounted for 26.3% of all deaths in South Africa in 2000. If the sexually transmitted diseases such as HIV/AIDS, which strike people while they are much younger, were reduced, it is likely that the proportion of South African deaths related to high BP would be closer to the worldwide estimates.



Table IV. Burden attributable to high blood pressure in males and females, South Africa, 2000

| Health outcome | Males | | Females | | Persons | |
|-------------------------------|-----------------|-------------------|-----------------|-------------------|-----------------|-------------------|
| | Deaths | DALYs | Deaths | DALYs | Deaths | DALYs |
| Ischaemic heart disease | 7 733 | 68 376 | 7 456 | 49 625 | 15 189 | 118 001 |
| Stroke | 6 898 | 69 481 | 10 426 | 90 395 | 17 324 | 159 876 |
| Hypertensive disease | 3 951 | 35 489 | 8 973 | 63 449 | 12 924 | 98 938 |
| Other cardiovascular diseases | 686 | 7 243 | 765 | 6 802 | 1 451 | 14 045 |
| Total | 19 268 | 180 589 | 27 620 | 210 271 | 46 888 | 390 860 |
| 95% uncertainty interval | 18 127 - 20 260 | 172 409 - 188 249 | 26 093 - 28 865 | 201 525 - 217 654 | 44 878 - 48 566 | 377 955 - 402 256 |
| % of total burden | 7.0% | 2.1% | 11.2% | 2.7% | 9.0% | 2.4% |
| 95% uncertainty interval | 6.6 - 7.4% | 2.0 - 2.2% | 10.6 - 11.7% | 2.6 - 2.8% | 8.6 - 9.3% | 2.3 - 2.5% |

DALYs = disability-adjusted life years.

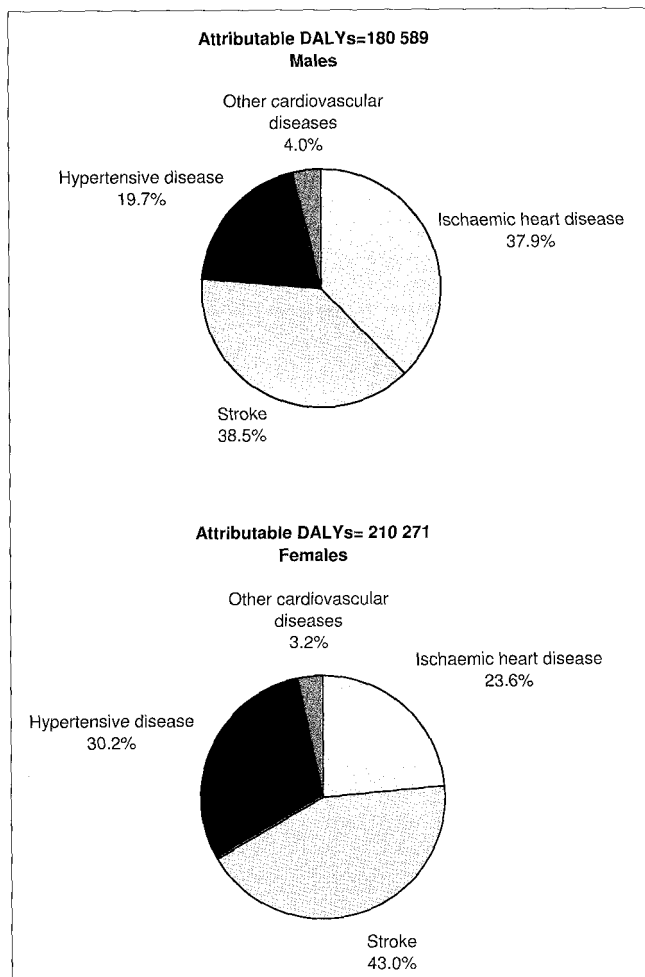


Fig. 1. Burden attributable to high blood pressure in males and females, South Africa, 2000.

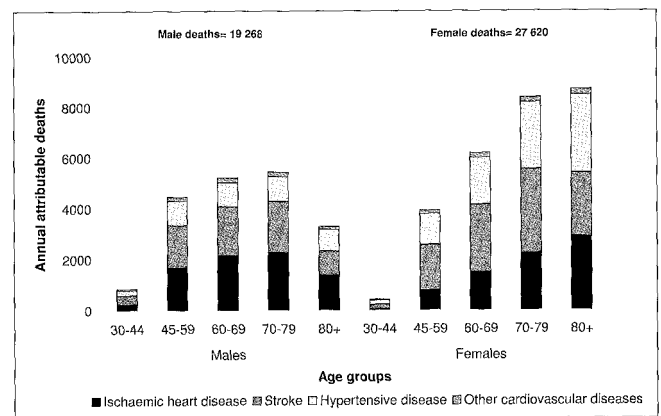


Fig. 2. Deaths attributable to high blood pressure for males and females by age group, South Africa, 2000.

among women. This would suggest that South African men may be further into the cardiovascular transition than women.

It is important to note that the hazard ratios¹⁵ used in this study are different from those used in the global study.¹ The RRs used in this analysis, obtained from the Prospective Studies Collaboration,¹⁵ are robust and reflect the best available evidence given the best available data and methods of analysis to hand (S Vander Hoorn, University of Auckland – personal communication, 2005). We have used the results from this meta-analysis since the evidence is based on a larger number of CVD events. The RRs used in these calculations are consistent with those used at the University of Auckland as well as in Australian CRA studies, and although there are some minor deviations in the RRs used from those reported in the WHO CRA chapter,¹ they do not differ substantially. Results obtained under the various possible RRs available for CVD do not vary greatly (data not shown).

A variety of population-based and personal interventions have been shown to be effective to reduce risk associated with suboptimal BP. Successful public health interventions combine multiple activities, resulting in synergistic effects to reduce the overall BP levels in the population as a whole. They require clear co-ordination, multiple messages from various organisations, and support from the food industry to reduce

The data are also consistent with global burden of disease estimates for the sub-Saharan African region, which show the overall burden of CVD deaths to be roughly split between stroke and IHD.²⁰ Furthermore, our results show interesting gender differences. High BP results in similar numbers of deaths and DALYs from stroke and IHD in men, but substantially higher burden from stroke compared with IHD



the salt content of staple foods in the country and to label food accordingly. Government action to reduce salt content of processed foods is a cost-effective way to limit CVD,²¹ and could reduce hypertension-related deaths. A recent randomised trial has demonstrated that modification of the salt content of a limited number of commonly consumed foods (that reduce the amount of sodium and increase the amount of potassium) lowered SBP by an average 6 mmHg in treated South African hypertensive patients from a low socio-economic setting (K Charlton, Medical Research Council – personal communication, 2007). On a population level, the BP-lowering effect of this dietary intervention would result in a 20% reduction in the number of deaths attributed to high BP, preventing more than 9 000 deaths in 1 year. In addition, prevention of excessive alcohol use and reduction of obesity in the population will further reduce BP.

In addition to the improved lifestyle factors to reduce BP, early diagnosis and cost-effective treatment with pharmacological agents are also necessary to reduce the disease burden associated with raised BP. The use of a multidrug regimen including two BP-lowering agents was found to be cost-effective for those with elevated absolute risk of CVD based on a risk-assessment tool including SBP.^{22,23} Regardless of treatment choice, guidelines defining eligibility for medication use must focus on absolute or global clinical risk, in which BP is one of many CVD risk factors assessed, instead of individual risk factor approaches.^{22,24}

The linear associations between BP and cholesterol levels as well as the degree of obesity and CVD in both developed and developing countries^{5,25} demonstrate the lack of a biological justification for the use of cut-off points, such as those that define hypertension. The absolute risk approach was also found to be more cost-effective in a model of BP control management in South Africa²⁶ by both preventing more CVD and reducing costs more than guidelines based on just treating those with a BP cut-off point of 140/90 mmHg. In that analysis it was estimated that the current South African clinical guidelines with a cut-off point of 140/90 mmHg cost an additional R180 million annually, compared with an approach of treating those with a 10-year absolute risk of CVD of 15% or greater. Furthermore, the current approach would result in 5 000 fewer quality-adjusted life years for the adult population in 10 years. A similar result was seen in Canada²⁷ when comparing the global risk approach with target levels of cholesterol for the basis of the treatment decision. In South Africa, approximately 2.6 million males and 3.3 million females (almost 6 million adults) would be classified as hypertensive with the current clinical cut-off point of 140/90 mmHg. A re-calculation of the attributable burden using the same RRs but a threshold of 140 mmHg, shows that 20% of the deaths attributable to high BP result from people with SBP between 115 mmHg and the clinical cut-off. Further research is needed

to identify a cost-effective approach to respond to this public health problem in our setting.

Conclusion

The data presented here show that poorly managed hypertension has a significant impact on the burden of disease in South Africa. Despite primary health care guidelines for the management of hypertension, data collected in 1998 suggest that the condition is poorly diagnosed and inadequately treated.^{6,8} This emphasises the need for improved BP control programmes that will simultaneously consider all the CVD risk factors in an integrated comprehensive chronic disease management programme. In addition, population-based strategies to reduce salt and increase potassium intake, limit alcohol intake and promote physical activity are needed.

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References

1. Lawes CMM, Vander Hoorn S, Law MR, Elliott P, MacMahon S, Rodgers A. High blood pressure. In: Ezzati M, Lopez AD, Rodgers A, Murray CJL, eds. *Comparative Quantification of Health Risks: Global and Regional Burden of Disease Attributable to Selected Major Risk Factors*. Geneva: World Health Organization, 2004: 281-390.
2. Prospective Studies Collaboration. Cholesterol, diastolic blood pressure, and stroke: 13 000 strokes in 45 000 people in 45 prospective cohorts. *Lancet* 1995; 346: 1647-1653.
3. Eastern Stroke and Coronary Heart Disease Collaborative Group. Blood pressure, cholesterol and stroke in eastern Asia. *Lancet* 1998; 352: 1801-1807.
4. Law MR, Wald NJ. Risk factor thresholds: their existence under scrutiny. *BMJ* 2002; 324: 1570-1576.
5. Department of Health, Medical Research Council and Macro International. *South African Demographic and Health Survey 1998, Full Report*. Pretoria: DOH, 2002.
6. Steyn K, Gaziano TA, Bradshaw D, Laubscher R, Fourie J. Hypertension in South African adults: results from the Demographic and Health Survey, 1998. *J Hypertens* 2001; 19: 1717-1725.
7. Steyn K, Jooste PL, Bourne L, et al. Risk factors for coronary heart disease in the black population of the Cape Peninsula. The BRISK study. *S Afr Med J* 1991; 79: 480-485.
8. Steyn K, Bradshaw D, Norman R, Laubscher R. Determinants and treatment of hypertension in South Africans during 1998. The first demographic and health survey. *S Afr Med J* (in press).
9. World Health Organization. *World Health Report 2002. Reducing Risks, Promoting Healthy Life*. Geneva: WHO, 2002.
10. Ezzati M, Lopez A, Rodgers A, Vander Hoorn S, Murray C. Selected major risk factors and global and regional burden of disease. *Lancet* 2002; 360: 1347-1360.
11. Bradshaw D, Groenewald P, Laubscher R, et al. *Initial Burden of Disease Estimates for South Africa, 2000*. MRC Technical Report. Parow: Medical Research Council, 2003.



12. Yarows SA, Brook RD. Measurement variation among 12 electronic home blood pressure monitors. *Am J Hypertens* 2000; 13: 276-282.
13. O'Brien E, Mee F, Atkins N, Thomas M. Evaluation of three devices for self-measurement of blood pressure according to the revised British Hypertension Society Protocol: the Omron HEM-705CP, Philips HP5332, and Nissei D5-175. *Blood Press Monit* 1996; 1: 55-61.
14. Stergiou GS, Voutsas AV, Achimastos AD, Mountokalakis TD. Home self-monitoring of blood pressure: is fully automated oscillometric technique as good as conventional stethoscopic technique? *Am J Hypertens* 1997; 10: 428-433.
15. Prospective Studies Collaboration. Age-specific relevance of usual blood pressure to vascular mortality: a meta-analysis of individual data for one million adults in 61 prospective studies. *Lancet* 2002; 360:1903-1913.
16. World Health Organization. *International Classification of Diseases. Manual of the International Statistical Classification of Diseases, Injuries, and Causes of Death, Based on the Recommendations of the Ninth Revision Conference in 1975*. Geneva: WHO, 1977.
17. MacMahon S, Peto R, Cutler J, et al. Blood pressure, stroke, and coronary heart disease. Part 1. Prolonged differences in blood pressure: Prospective observational studies corrected for the regression dilution bias. *Lancet* 1990; 335: 765-774.
18. Norman R, Bradshaw D, Schneider M, Pieterse D, Groenewald P. *Revised Burden of Disease Estimates for the Comparative Risk Factor Assessment, South Africa 2000*. MRC Technical Report. Parow: Medical Research Council, 2006. <http://www.mrc.ac.za/bod/bod.htm> (last accessed 18 January 2007).
19. Palisade Corporation. @RISK software version 4.5 for Excel. New York: Palisade Corporation, 2002.
20. Murray CJL, Lopez AD, Mathers CD, Stein C. *The Global Burden of Disease 2000 Project: Aims, Methods and Data Sources*. Geneva: World Health Organization, 2000. GPE Discussion Paper No 36, 2001. <http://www.who.int/healthinfo/discussionpapers/en/index.html>. WHO Global Burden of Disease study for 2000, Version 1 results. <http://www.who.int/healthinfo/bodgbd2000v1/en/index.html> (last accessed 18 January 2007).
21. Murray CJL, Lauer JA, Hutubessy RC, et al. Effectiveness and costs of interventions to lower systolic blood pressure and cholesterol: a global and regional analysis on reduction of cardiovascular risk. *Lancet* 2003; 361: 717-725.
22. Gaziano TA, Opie LH, Weinstein MC. Cardiovascular disease prevention with a multidrug regimen in the developing world: a cost-effectiveness analysis. *Lancet* 2006; 368: 679-686.
23. Rogers A, Lawes CMM, Gaziano T, Vos T. The growing burden of risk from high blood pressure, cholesterol and bodyweight. In: Jamison DT, Breman JG, Measham AR, et al., eds. *Disease Control Priorities in Developing Countries*. 2nd ed. Washington: Oxford University Press and The World Bank, 2006.
24. Jackson R, Lawes CMM, Bennett DA, Milne RJ, Rodgers A. Treatment with drugs to lower blood pressure and blood cholesterol based on an individual's absolute cardiovascular risk. *Lancet* 2005; 365: 434-441.
25. Yusuf S, Hawken S, Ounpuu S, et al. Effect of potentially modifiable risk factors associated with myocardial infarction in 52 countries (the INTERHEART study): case-control study. *Lancet* 2004; 364: 937-952.
26. Gaziano TA, Steyn K, Cohen DJ, Weinstein MC, Opie LH. Cost-effectiveness analysis of hypertension guidelines in South Africa: Absolute risk versus blood pressure level. *Circulation* 2005; 112: 3569-3576.
27. Manuel DG, Lim J, Tanuseputro P, et al. Revisiting Rose: strategies for reducing coronary heart disease. *BMJ* 2006; 332: 659-662.